(19) World Intellectual Property Organization International Bureau



(43) International Publication Date 2 June 2005 (02,06,2005)

PCT

(10) International Publication Number WO 2005/049618 A1

(51) International Patent Classification⁷:

(21) International Application Number:

PCT/EP2004/012655

C07D 491/04

(22) International Filing Date:

9 November 2004 (09.11.2004)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

103 53 999.9

19 November 2003 (19.11.2003) DE

- (71) Applicant (for all designated States except US): DSM IP ASSETS B.V. [NL/NL]; Het Overloon 1, NL-6411 TE Heerlen (NL).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): FISCHESSER, Jocelyn [FR/FR]; 34a, rue d'Illzach, F-68270 Wittenheim (FR). FRITSCH, Helmut [DE/DE]; Hasenweg 13, 79540 Lörrach (DE). GUM, Andrew, George [US/FR]; 4, rue des Pierres, F-68170 Rixheim (FR). KARGE, Reinhard [DE/DE]; Belchenring 3, 79219 Staufen (DE). KEUPER, Ralf [DE/DE]; Tüllinger Strasse 23a, 79541 Lörrach (DE).
- (74) Agents: PANES, Nigel et al.; c/o DSM Nutritional Products Ltd., Wurmisweg 576, CH-4303 Kaiseraugst (CH).

- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR). OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: MANUFACTURE OF VITAMIN B6

(57) Abstract: A process for manufacturing a 3-unsubstituted, 3-monosubstituted or 3,3-disubstituted 9-acyloxy-1,5-dihydro-8-methylpyrido[3,4-e] [1,3]dioxepin (I) and optionally for manufacturing pyridoxine involves performing an addition reaction between a 4-methyl-5-alkoxy-oxazole (II) and a 2-unsubstituted, 2-monosubstituted or 2,2-disubstituted 4,7-dihydro-(1,3)-dioxepin (III) in the substantial absence of a solvent and a catalyst to give a product mixture consisting essentially of the appropriate Diels-Alder adduct (IV) in a major proportion and the appropriate 3-unsubstituted, 3-monosubstituted or 3,3-disubstituted 1,5-dihydro-8-methylpyrido[3,4-e] [1,3]dioxepin 9-ol (V) in a minor proportion, removal of a substantial proportion of the unreacted oxazole and dioxapin starting materials from the product mixture by distillation under reduced pressure, addition of a substantially anhydrous organic acid to said product mixture and rearrangement of the Diels-Alder adduct IV to further V in the presence of said substantially anhydrous organic acid with removal of the generated alkanol by distillation under reduced pressure, and acylation of the resultingly enriched quantity of V with an added carboxylic acid anhydride to produce the desired I, and optionally converting this so-manufactured acylation product I to pyridoxine by acid hydrolysis for achieving deprotection and deacylatiom. Pyridoxine is a well known form of vitamin B₆ with well established utility.

BEST AVAILABLE COPY

